PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Applicant's or agent's file reference see form PCT/ISA/220	Date of mailing *(day/month/year)* see form PCT/ISA/210 (second sheet) **FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US2005/044215	06.12.2005	07.12.2004

International Patent Classification (IPC) or both national classification and IPC
INV. C07K14/57 G01N33/68 A61K38/21 A61K39/00 C12N15/23 C12N15/63

Applicant
THE ARIZONA BOARD OF REGENTS, A BODY CORPORATE ACT

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☒ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:	Date of completion of this opinion	Authorized Officer
European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	see form PCT/ISA/210	Schmidt, Harald Telephone No. +31 70 340-4023

Form (PCT/ISA/237) (Cover Sheet) (April 2005)

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US2005/044215

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of:

   ☒ the international application in the language in which it was filed

   ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1 (b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

      ☒ a sequence listing

      ☐ table(s) related to the sequence listing

   b. format of material:

      ☒ on paper

      ☒ in electronic form

   c. time of filing/furnishing:

      ☒ contained in the international application as filed.

      ☐ filed together with the international application in electronic form.

      ☒ furnished subsequently to this Authority for the purposes of search.

3. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of

☐ the entire international application

☒ claims Nos. 2-4,24-26 (completely), 5-23 (partially) and 9-23 with respect to IA

because:

☒ the said international application, or the said claims Nos. 9-23 with respect to IA relate to the following subject matter which does not require an international search *(specify)*:

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed *(specify)*:

☒ no international search report has been established for the whole application or for said claims Nos. 2-4,24-26 (completely) and 5-23 (partially)

☐ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

- ☐ furnish a sequence listing on paper complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.
- ☐ furnish a sequence listing in electronic form complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.
- ☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rules 13*ter*.1(a) or (b).

☐ a meaningful opinion could not be formed without the tables related to the sequence listings; the applicant did not, within the prescribed time limit, furnish such tables in electronic form complying with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions, and such tables were not available to the International Searching Authority in a form and manner acceptable to it.

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in electronic form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See Supplemental Box for further details

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US2005/044215

Box No. IV Lack of unity of invention

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees, the applicant has, within the applicable time limit:

   ☐ paid additional fees

   ☐ paid additional fees under protest and, where applicable, the protest fee

   ☐ paid additional fees under protest but the applicable protest fee was not paid

   ☒ not paid additional fees

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is

   ☐ complied with

   ☒ not complied with for the following reasons:

   see separate sheet

4. Consequently, this report has been established in respect of the following parts of the international application:

   ☐ all parts.

   ☒ the parts relating to claims Nos. 1 (completely) and 5-23 (partially)

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	18-20,22,23
	No:	Claims	1,5-17,21
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1,5-23
Industrial applicability (IA)	Yes:	Claims	1,5-8
	No:	Claims	

2. Citations and explanations

   see separate sheet

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US2005/044215

Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claims 9 to 23 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Claims 2-4,24-26 (completely) and 5-23 (partially) relate to inventions 2 to 151, which have not been searched due to the lack of unity (see under Item IV).

Re Item IV

Lack of unity of invention

This Authority considers that there are 151 inventions covered by the claims indicated as follows:

I: Claims 1 (completely) and 5-23 (partially) directed to polypeptides according to formula 1
II: Claims 2 (completely) and 5-23 (partially) directed to polypeptides according to formula 2
Inventions 3-151: Claims 3,4,24-26 (completely) and 5-23 (partially) directed to polypeptides according to SEQ ID NO: 1,2,3....,148 or 149

The reasons for which the inventions are not so linked as to form a single general inventive concept, as required by Rule 13.1 PCT, are as follows:
The problem to be solved by the present application resides in the provision of compounds for treatment of diseases by stimulating immune system activity, including infection, tumor, bone diseases and pain.
As a solution, polypeptide mimetics of GalNAc are provided.
The technical feature in the sense of Rule 13.2 PCT which a priori could unify different solutions is the entity of being a polypeptide mimetic of GalNAc.
However, such a solution has already been proposed in the prior art, see e.g. the

international patent application WO 96/40903 disclosing macrophage activating factors derived from Vitamin D binding protein (DBP) for the treatment of cancer, infection, osteoporosis and for use as an adjuvant for immunization and vaccination (see page 1) or the international patent application WO 02/058589 disclosing a DBP peptide comprising an N-acetyl galactosamine for use in promoting bone deposition (see claims 1-3,5,9-11, pages 4,5 and Figure 1), or the international patent application WO 2004/011650 disclosing the peptide MDSSTPPPSGWSFS falling within the scope of formula 1 of the present application for use in the treatment of infections (see table 2E, pages 1-4, claim 27).

The problem to be solved may therefore be considered to be the provision of further polypeptide mimetics of GalNAc.

However, a structural relationship among the polypeptides of the different subjects which could fulfil the role of a "special technical feature" in the sense of Rule 13.2 PCT is missing.

As there are no other special technical features, the present application is found to lack unity of invention, giving rise to the subjects as defined.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

D1: WO 2004/011650 A (INTERCELL AG; MATTNER, FRANK; SCHMIDT, WALTER; HABEL, ANDRE) 5 February 2004 (2004-02-05)

D2: WO 96/40903 A (YAMAMOTO, NOBUTO) 19 December 1996 (1996-12-19)

D3: WO 02/058589 A (NORTHEASTERN OHIO UNIVERSITIES COLLEGE OF MEDICINE; SCHNEIDER, GARY, B) 1 August 2002 (2002-08-01)

D4: US-A-5 641 747 (POPOFF ET AL) 24 June 1997 (1997-06-24)

Novelty

The document D1 discloses the peptide MDSSTPPPSGWSFS for the treatment of

infections (see table 2E, pages 1-4 and claim 27).
Therefore, the subject-matter of independent claims 1, 5-9,17 and 21 does not meet the requirements of Article 33(2) PCT.

Inventive step

The document D2 is considered to represent the closest prior art for the subject-matter of independent claims 18-20,22 and 23 and discloses macrophage activating factors derived from Vitamin D binding protein (DBP) for the treatment of cancer, infection, osteoporosis and for use as an adjuvant for immunization and vaccination (see page 1).
The subject-matter of independent claims 18-20,22 and 23 differs in that other amino acid sequences are used.
The problem to be solved resides in the provision of further polypeptides for the treatment of cancer, bone disorders, pain and for the use as an adjuvant for immunisation and vaccination.
However, the use of further polypeptides derived from Vitamin D binding protein (DBP) is a routine option and therefore obvious for the skilled person, particular with view to the fact that the present application does not provide any experimental data making it plausible that the claimed polypeptides may be capable of treating cancer, bone disorders, pain, and may be used as an adjuvant for immunisation and vaccination.
Hence, the subject-matter of claims 18-20,22 and 23 does not involve an inventive step in the sense of Rule 33(3) PCT.

Dependent claims 10-16 do not contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of novelty and/or inventive step, see documents D1 to D4 and the corresponding passages cited in the search report.

Industrial applicability

For the assessment of the present claims 9 to 23 on the question whether they are

industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Re Item VII

Certain defects in the international application

Claim 5 refers inter alia to subsequent claims 6-14.

The expression "in a third aspect, the present invention provides" in claim 3 is redundant.